UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/836,439	04/17/2001	Therese de Bizemont	017753-154	5851

21839 7590 09/24/2002

BURNS DOANE SWECKER & MATHIS L L P
POST OFFICE BOX 1404
ALEXANDRIA, VA 22313-1404

EXAMINER	
SCHNIZER, RICHARD A	

ART UNIT	PAPER NUMBER
1635	14

DATE MAILED: 09/24/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/836,439	Applicant(s) DE BIZEMONT ET AL.	
	Examiner Richard Schnizer	Art Unit 1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-39 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) 1-39 are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Election/Restriction

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-21, drawn to methods of delivering an oligonucleotide *in vivo* to cells of an animal by iontophoresis, classified in class 435, subclass 455.

II. Claims 22-24, drawn to methods of treating a disease in an animal by delivering by iontophoresis a chimeric oligonucleotide to cells of the animal, classified in class 514, subclass 44.

III. Claim 25 and 26 drawn to methods of making an animal model by administering by iontophoresis a chimeric oligonucleotide to cells of the animal, classified in class 800, subclass 9.

IV. Claims 27, 28, 32, and 37, drawn to chimeric oligonucleotides for reverting a C to A transversion at codon 347 of a gene encoding murine cGMP phosphodiesterase beta subunit, classified in class 536, subclass 23.1.

V. Claims 29 and 38, drawn to a chimeric oligonucleotide capable of inducing a nonsense mutation in DNA encoding murine or human transcription factor HIF1alpha such that the subsequently encoded protein is nonfunctional, classified in class 536, subclass 23.1.

VI. Claims 30 and 39, drawn to a chimeric oligonucleotide capable of reverting a mutation in DNA encoding human RP1 protein, said mutation being responsible for the expression of a non-functional protein, classified in class 536, subclass 23.1.

VII. Claims 30 and 39, drawn to a chimeric oligonucleotide capable of reverting a K296E mutation in a gene encoding human opsin, classified in class 536, subclass 23.1.

VIII. Claim 31, drawn to a chimeric oligonucleotide for introducing a mutation into a human RP1 gene, said mutation being responsible for the expression of a non-functional protein, classified in class 536, subclass 23.1.

IX. Claim 31, drawn to a chimeric oligonucleotide capable of introducing a K296E mutation into murine opsin, classified in class 536, subclass 23.1.

X. Claim 31, drawn to a chimeric oligonucleotide capable of introducing a E348-STOP mutation into murine RP1, classified in class 536, subclass 23.1.

XI. Claim 31, drawn to a chimeric oligonucleotide capable of reverting a K296E mutation in murine opsin, classified in class 536, subclass 23.1.

XII. Claim 31, drawn to a chimeric oligonucleotide capable of reverting a E348-STOP mutation in murine RP1, classified in class 536, subclass 23.1.

XIII. Claim 33, drawn to a method to treat a human having retinopathy induced by a mutation in RP1 comprising contacting in vivo the human's genomic DNA with a

chimeric oligonucleotide capable of reverting a mutation in human RP1, classified in class 514, subclass 44.

XIV. Claim 34, drawn to a method of treating a human with ocular neovascularization induced by expression of the normal transcription factor HIF1alpha gene, comprising contacting in vivo the human's genomic DNA with a chimeric oligonucleotide capable of inducing a nonsense mutation rendering the encoded HIF1alpha nonfunctional, classified in class 514, subclass 44.

XV. Claims 35 and 36, drawn to an animal model comprising a mutation in the RP1 gene, classified in class 800, subclass 9.

Claims 1-21 are generic to a plurality of patentably distinct inventions listed as groups I-III. If any of these groups is elected, the claims will be examined to the extent that they are defined by the elected group.

Invention I is related to inventions II and III as a combination and subcombinations. Inventions in this relationship are distinct if it can be shown that (1) the combination as claimed does not require the particulars of the subcombination as claimed for patentability, and (2) that the subcombination has utility by itself or in other combinations (MPEP § 806.05(c)). In the instant case, the combination as claimed does not require the particulars of the subcombination as claimed because the method of group I need not be used for disease treatment or for making an animal model, rather it may be used for studying gene function in vivo. The subcombinations have separate utilities as listed, i.e. for disease treatment and for making animal models.

The method of group I is related to the methods of groups II and III because it must be used in these methods. The inventions are distinct because the method of group I need not be used for disease treatment or making an animal model, but rather may be used for other purposes such as from the invention.

The inventions of groups II and III are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the two methods lead to different results, i.e. disease treatment and the development of an animal model. The specification does not disclose thes methods as capable of use together, and they have different effects as noted above.

Inventions I and II are related to inventions XIII and XIV as combinations and subcombinations. Inventions in this relationship are distinct if it can be shown that (1) the combination as claimed does not require the particulars of the subcombination as claimed for patentability, and (2) that the subcombination has utility by itself or in other combinations (MPEP § 806.05(c)). In the instant case, the combinations as claimed does not require the particulars of the subcombinations as claimed. For example, none of the inventions of groups I-III requires the treatment of retinopathy (group XIII) or neovascularization (group XIV), and neither of groups XII or XIV requires iontophoresis. The subcombinations have separate utilities as listed, i.e. for treatment of specific diseases.

Inventions I and III are related to invention XV as processes of making and product made. The inventions are distinct if either or both of the following can be shown: (1) that the process as claimed can be used to make other and materially different product or (2) that the product as claimed can be made by another and materially different process (MPEP § 806.05(f)). In the instant case the methods of groups I and III can be used to make animal models of diseases other than those caused by RP1 mutation, as required by group XV. Furthermore, the invention of group XV is product by process claim directed to an animal model that can be made by different processes, i.e. by delivery of chimeric oligonucleotides in the absence of an electroporation step. Alternatively the product animal can be made through standard transgenic technology.

Invention II is unrelated to invention XV. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case invention II does not result in the animal model of group XV, and the animal model is not used in the method of invention II. Thus the methods are not disclosed as capable of use together, and have different functions and effects.

Invention III is unrelated to inventions XIII and XIV. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case invention III does not result in the treatment of any disease, as required by

inventions XIII and XIV. Thus the methods are not disclosed as capable of use together, and have different functions and effects.

Inventions I-III, XIII, and XIV are related to inventions IV-XII as processes for using products and products capable of use in the processes. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product (MPEP § 806.05(h)). In the instant case the methods can be performed using oligonucleotides other than those disclosed, and the products can be used for purposes other than in vivo methods, such as in vitro methods of studying gene function.

The oligonucleotides of inventions IV-XII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the different inventions have different structures and functions which give different modes of operation and effects, and the oligonucleotides are not disclosed as useful together in the same method. For example, none of the oligonucleotides of the various groups has the same nucleotide sequence, and each oligonucleotide introduces a base change which has a different effect on the protein encoded by the target gene.

Invention XV is unrelated to inventions IV, V, VII, and IX-XI. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different

modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the oligonucleotides of groups IV, V, VII, IX-XI, and XIII cannot be used to make the animal model of group XV, and the animal model of group XV cannot be used to produce mutations induced by the oligonucleotides of inventions IV, V, VII, IX-XI, and XIII. These products have different functions and effects and are not disclosed as useful together.

Invention XV is related to the oligonucleotides of inventions VI, VIII, and XII, because these oligonucleotides can be used to either make the model, or to repair the model. The inventions are distinct because the oligonucleotides can be used for other purposes such as studying gene function in *in vitro* cellular systems.

Inventions XIII and XIV are unrelated because they require different outcomes and different method steps. Inveniton XIII requires treatment of retinopathy induced by mutation in RP1, whereas invention XIV requires treatment of ocular neovascularization by suppressing HIF1alpha expression. The methods cannot be used to effect the same outcome and emply different reagents and method steps. Thus the methods are not disclosed as capable of use together, and have different modes of operation, different functions, and different effects

The methods of treatment of nventions XIII and XIV are unrelated to the animal model of invention XV. The methods of inventions XIII and XIV do not result in the production of an animal model of with a mutation in the RP1 gene, and the animal model cannot be used in the methods of treatment of groups XIII and XIV.

Because these inventions are distinct for the reasons given above, have acquired a separate status in the art as shown by their different classification and their recognized divergent subject matter, and because each invention requires a separate, non-coextensive search, restriction for examination purposes as indicated is proper.

Applicant is advised that the response to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a petition under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(I).

Any inquiry concerning this communication or earlier communications from the examiner(s) should be directed to Richard Schnizer, whose telephone number is 103-306-5441. The examiner can normally be reached Monday through Friday between the hours of 6:20 AM and 3:50 PM. The examiner is off on alternate Fridays, but is usually in the office anyway.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John Leguyader, can be reached at 703-308-0447. The FAX numbers for art unit 1632 are 703-308-4242, and 703-305-3014. Additionally correspondence can be transmitted to

the following RIGHTFAX numbers: 703-872-9306 for correspondence before final rejection, and 703-872-9307 for correspondence after final rejection.

Inquiries of a general nature or relating to the status of the application should be directed to the Patent Analyst Trina Turner whose telephone number is 703-305-3413.

Richard Schnizer, Ph.D.

JAMES KETTER
PRIMARY EXAMINER